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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/665,864	09/18/2003	**Zhuyin Julie Li**	USA V2002/0121 US NP	8381

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EXAMINER	
KIM, TAEYOON	
ART UNIT	**PAPER NUMBER**
1651	

NOTIFICATION DATE	DELIVERY MODE
10/16/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/665,864	LI ET AL.	
	Examiner	Art Unit	
	TAEYOON KIM	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Applicant's amendment and response filed on 7/3/2008 has been received and entered into the case.

Claims 1-25 are pending and have been considered on the merits. All arguments have been fully considered.

Response to Arguments

In the response to the previous office action, applicant argued that the office action failed to establish a prima facie case of obviousness for any of the pending claims. Particularly, applicant asserted that the claimed invention is a simple assay with remarkably short duration time, and the references in the claim rejection under 35 U.S.C.§103 do not teach a simple screening assay or suggest the desirability. Furthermore, Decker et al. (primary reference in 35 U.S.C.§103 rejection) teach a multiple step method which requires repetitive washing steps, and long duration time, and the secondary references do not remedy the deficiencies of Decker et al.

This argument is not persuasive. First of all, applicant failed to prove that the claimed invention remarkably shorten the assay duration time over the prior art. Particularly, the claims disclose that the incubation time for step (a) has duration of as short as about 10 minutes. This limitation is considered as open end and interpreted that the duration can be 10 minutes or more (claim 2, 7, 15, 20 and 22). Claims 3, 10, 16 and 21 disclose the duration of incubation being about 10 min. to about 2 hrs. This limitation is met by the incubation duration of 1 hr as taught by Decker et al.

The basis of applicant's argument is that there are multiple washing steps in the method of Decker et al. and therefore the multiple steps cause longer assay time than the claimed invention. As discussed in the previous office action, the duration of assay can be routinely optimized by a person of ordinary skill in the art, and the washing steps can be easily modified and shortened by using various known means in the art.

The argument by applicant on the method of Decker et al. is mainly the long reaction time (overnight or at least more than 7 hours). This is because the step of immobilizing PARP on the substrate. This step should not be included in the total reaction time because it is preparation for the incubating PARP with NAD, which is not required by the claimed invention. Thus, the incubation duration of PARP with NAD per se is only 1 hr as shown in Fig. 1 of Decker et al.

Furthermore, by combining the teaching of Corominas et al., which teach the use of labeled NAD, the duration of assay would be shortened for the method of Decker et al. Decker et al. utilize antibodies conjugated peroxidase, requiring further incubation time, and upon using the labeled NAD of Corominas et al. the primary and secondary antibody incubation time and washing steps in between are not required, and thus, the overall assay duration would be clearly shortened. It is extremely well known in the art the use of directly labeled molecules in an assay to shorten the assay time. That would be a good motivation to a person of ordinary skill in the art to combine the teaching of Decker et al. with Corominas et al.

Similarly, the combining the method of Trevigen with Armstrong et al., the asserted long duration time can be easily shortened, and upon the using of the labeled

NAD, multiple washing steps which may be involved in ELISA would not be necessary.

Applicant argued that the method of Trevigen teaches away from the claimed invention. It is not clear what basis applicant concludes that the method of Trevigen teaches away. It is a desire of a person of ordinary skill in the art to make an assay system efficient with optimal outcome, and it is extremely well known in the art that by replacing the ELISA step of Trevigen with the labeled NAD of Armstrong et al., the time required for several steps in ELISA would be eliminated and thus, the overall duration would be shortened. Therefore, a person of ordinary skill in the art would utilize the labeled NAD of Armstrong et al. in the method of Trevigen to make the assay system efficient and less time-consuming one.

The main gist of the current invention over the prior art is the use of fluorescence-labeled NAD, which eventually reduces duration time of the claimed method. Since it is extremely well known in the art that fluorescence-labeled substrate provides a faster and easier alternative technique to the conventional antibody based detection system such as ELISA as taught by Corominas et al., Armstrong et al., or Sundberg, a person of ordinary skill in the art would have a strong motivation to use fluorescence-labeled NAD in the method of Decker et al. or Trevigen to detect PARP.

Therefore, the claim rejections under 35 U.S.C.§103 are still maintained.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-25 stand rejected under 35 U.S.C. 103(a) as being unpatentable over

Decker et al. (Clin. Caner Res. 1999) in view of Corominas et al. (JBC, 1985) and Armstrong et al. (Anal. Biochem. 2001).

Decker discloses a PARP inhibition assay which differs from that recited in the claims in that Decker does not use fluorescently labeled NAD in the quantification of enzyme activity. See, e.g., Fig 1, on page 1170. However, Corominas et al. clearly discloses that labeled NAD can be used in the quantification of PARP activity. See, e.g., page 16270, left column. Moreover, Armstrong discloses the use of fluorescently labeled NAD in an assay of ADP-ribosylating enzyme, an assay which detects similar activity to that of both Decker and Corominas. See, e.g., page 28. Thus, the artisan of ordinary skill would have considered it obvious to have used fluorescently labeled NAD in the quantification of enzyme activity in Decker's assay, motivation for such practice being derived from Corominas' disclosure of the suitability of labeled NAD as detection moiety in PARP assays, and from Armstrong's disclosure of the suitability of fluorescently labeled NAD as a detection moiety in a similar assay of ADP-ribosylating enzyme. Moreover, the selection of known fluorescent moieties, and the determination of suitable linking moieties therefor as recited in the claims under examination, would have been considered obvious in view of the cited references' disclosures of the suitability of using fluorescently labels to detect NAD. A holding of obviousness is therefore required.

Claims 1-25 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Trevigen (Universal Colorimetric PARP Assay kit with histones and coating buffer, 2000; http://www.trevigen.com/Protocols/4671_4672-096-K.pdf) in view of Armstrong et al.

(supra), Sundberg (Current Opinion in Biotechnology, 2000, 11:47–53) and Human Molecular Genetics (Fluorescence labeling and detection system, 1999; http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hmg.table.479)

It is noted that although the published date of the Trevigen article is not clearly established, this assay kit utilizing a biotinylated NAD+ for PARP assay has been disclosed by an article entitled to New Technology (Nature Medicine, 2000, 6:715;). Therefore, the Examiner considers the reference as a prior art to the filing date of the current application.

The Trevigen reference teaches a method of determining inhibitors on the activity of PARP comprising steps of incubation of PARP enzyme, an inhibitor, a substrate (biotinylated NAD+, DNA, histone), detection of enzymatic activity, and comparison of the measurement (see pages 1-4).

The Trevigen article does not teach the use of fluorescently labeled NAD+ in an assay.

Armstrong et al. teach the use of fluorescently labeled NAD in an assay of ADP-ribosylating enzyme.

Sundberg teaches fluorescence-based biochemical assays.

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to substitute biotinylated NAD+ of Trevigen with fluorescently labeled NAD+ of Armstrong et al. in the method of Trevigen Instruction.

The skilled artisan would have been motivated to make such a modification because Sundberg teach that fluorescence-based detection methods are inherently

sensitive due to the short duty cycle of most fluorophores (the fluorescence lifetime of fluorescein is ~4 ns) and consequently high emitted photon fluxes that can be achieved even with modest excitation light sources. This property, combined with the variety of different fluorescence modes that can be exploited to advantage in homogeneous assay formats, makes fluorescence detection highly amenable to many high-throughput screening applications (see page 47, right column).

The person of ordinary skill in the art would have had a reasonable expectation of success in substituting biotinylated NAD+ with fluorescence-labeld NAD+ because fluorescence labeling has been well known and practiced in the art.

M.P.E.P. §2144.06 states "In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. In re Ruff, 256 F.2d 590, 118 USPQ 340 (CCPA 1958) (The mere fact that components are claimed as members of a Markush group cannot be relied upon to establish the equivalency of these components. However, an applicant's expressed recognition of an art-recognized or obvious equivalent may be used to refute an argument that such equivalency does not exist.); In re Scott, 323 F.2d 1016, 139 USPQ 297 (CCPA 1963)."

Therefore, the substitution of biotinylation from Trevigen Instruction of the fluorescently labeled NAD+ of Armstrong et al. in an assay of ADP-ribosylating enzyme would have been obvious because Sundberg discloses colorimetric, fluorescent or luminescent read-out as an alternative method for a detection/quantification system (p.

49, right column). Therefore, these may be considered to be art-accepted equivalents.

In addition, various different fluorescence labels such as Texas red, rhodamine, or CyDye are well known equivalents for fluorescent labeling of chemicals as supported by Human Molecular Genetics (supra).

One of skill in the art would have been motivated at the time of invention to make this substitution in order to quantify the PARP activity as suggested by Trevigen with a reasonable expectation of success. The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references.

Furthermore, it would have been obvious to a person of ordinary skill in the art to try different labels available in the art as a detection means, and there are a known number of alternatives/equivalent dyes or labels suitable for the purpose of labeling a molecule.

The Supreme Court recently states in KSR v. Teleflex (550 US82 USPQ2d 1385, 2007) "The same constricted analysis led the Court of Appeals to conclude, in error, that a patent claim cannot be proved obvious merely by showing that the combination of elements was "obvious to try." Id., at 289 (internal quotation marks omitted). When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under §103."

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TAEYOON KIM whose telephone number is (571)272-9041. The examiner can normally be reached on 8:00 am - 4:00 pm ET (Mon-Thu).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford/
Primary Examiner, Art Unit 1651

Taeyoon Kim